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Dated: December 30, 2010 Signature: /Thomas J. Engellenner/ (Thomas J. Engellenner)

Docket No.: 105447-2 (PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Anthony Atala et al.

Application No.: 10/766,642 Confirmation No.: 4621

Filed: January 28, 2004 Art Unit: 1651

For: Enhancement Of Angiogenesis To Grafts Using Cells Engineered To Produce Growth Factors Examiner: Allison M Ford

PETITION PURSUANT TO 37 CFR §1.144 FOR REVIEW OF A REQUIREMENT FOR RESTRICTION

Attn: Director of Technology Center 1600
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR §1.144, Applicants hereby petition for reconsideration of the restriction requirement asserted by Examiner Ford in an Office Action dated March 30, 2010, as maintained in the Advisory Action dated July 15, 2010.

A Listing of the Claims begins on page 2 of this petition.

Remarks begin on page 6 of this petition.

LISTING OF THE CLAIMS

1. (Previously presented) A method of organ augmentation comprising the steps of:

transiently transfecting a first population of cells with a plasmid encoding the angiogenesis modulating agent VEGF;

selecting a second population of cells to be assimilated at a target tissue region upon implantation,

suspending the first population of cells and the second population of cells in an injectable polymer matrix;

injecting the first population of cells and the second population of cells and the polymer matrix into the target tissue region where the first population of cells will express the VEGF angiogenesis modulating agent, thereby inducing assimilation and differentiation of the second population of cells in the target region and augmenting organ function.

2. (Previously Presented) The method of claim 1, wherein the step of transfecting the first population of cells comprises transiently transfecting the cells such that the angiogenesis modulating agent is produced for less than three weeks.

3. (Previously Presented) The method of claim 1, wherein the first population of cells comprises undifferentiated cells.

4. (Previously Presented) The method of claim 1, wherein the first population of cells comprises vascular endothelial cells (EC).

5. (Canceled)

6. (Previously Presented) The method of claim 1, wherein the second population of cells comprises myoblasts.

7. (Withdrawn) The method of claim 1, wherein the second population of cells comprises endothelial progenitor cells (EPC).

8. (Previously Presented) The method of claim 1, wherein the polymer matrix comprises collagen.

9. (Previously Presented) The method of claim 8, wherein the polymer matrix comprises collagen type I.

10. (Previously Presented) The method of claim 1, wherein the step of transiently transfecting the first population of cells further comprises:

encapsulating the transfected first population of cells;

suspending the encapsulated first population of cells and the second population of cells in an injectable polymer matrix

injecting the encapsulated first population of cells and the second population of cells and the polymer matrix into the target tissue region where the encapsulated first population of cells will express the VEGF angiogenesis modulating agent, thereby inducing assimilation and differentiation of the second population of cells in the target region and augmenting organ function.

11. (Canceled)

12. (Previously Presented) The method of claim 1, wherein the first population of cells comprises myoblasts.

13.–22.(Canceled)

23. (Previously presented) A method for augmenting organ function comprising:

transiently transfecting a first population of cells with a plasmid encoding an angiogenesis modulating agent;

culturing at least a second population of cells on a matrix material to produce an organ construct, wherein the second population of cells comprises cells of a different cell type than the first population; and

implanting the organ construct and the first population of cells *in vivo* at a target site to replace or augment organ function, such that the first population of cells express

the angiogenesis modulating agent thereby inducing the second population of cells to assimilate and differentiate at the target site.

24. (Original) The method of claim 23, wherein the matrix is decellularized tissue.

25. (Original) The method of claim 23, wherein the matrix is a hydrogel.

26. (Original) The method of claim 23, wherein the matrix is a polymer.

27. (Canceled)

28. (Original) The method of claim 23, wherein the angiogenesis modulating agent is VEGF.

29. (Previously Presented) The method of claim 23, wherein the method further comprises assimilating the first population of cells into a tissue layer.

30.-32.(Canceled)

33. (Previously Presented) The method of claim 23, wherein the step of transiently transfecting the first population of cells further comprises:

encapsulating the transfected first population of cells and

implanting the organ construct and the encapsulated first population of cells *in vivo* at the target site to replace or augment organ function such that the first population of cells express the angiogenesis modulating agent and the second population of cells assimilate and differentiate at the target site.

34. (Previously Presented) The method of claim 10, wherein the step of encapsulating the transfected first population of cells further comprises using microspheres.

35. (Previously Presented) The method of claim 10, wherein the step of encapsulating the transfected first population of cells further comprises using alginate-PLL capsules.

36. (Previously Presented) The method of claim 33, wherein the step of encapsulating the transfected first population of cells further comprises using microspheres.

37. (Previously Presented) The method of claim 33, wherein the step of encapsulating the transfected first population of cells further comprises using alginate-PLL capsules.

38. (Withdrawn) The method of claim 1, wherein the first population of cells comprises endothelial progenitor cells.

39. (Withdrawn) The method of claim 23, wherein the first population of cells comprises endothelial progenitor cells.

40. (Previously Presented) The method of claim 23, wherein the first population of cells comprises vascular endothelial cells (EC).

41. (Previously Presented) The method of claim 23, wherein the first population of cells comprises myoblasts.

42. (Withdrawn) The method of claim 23, wherein the second population of cells comprises endothelial progenitor cells.

43. (Previously Presented) The method of claim 23, wherein the second population of cells comprises myoblasts.

REMARKS

Applicants hereby petition for reconsideration of the restriction requirement asserted by Examiner Ford in an Office Action dated March 30, 2010, as maintained in the Advisory Action dated July 15, 2010. The March 30th restriction requirement should be withdrawn and claims 7, 38-39 and 42 should be examined on their merits because the Examiner's argument that the subject matter of these claims was "constructively withdrawn" is incorrect. To the contrary, Applicants' amendment to claim 7 and the presentation of claims 38-39 and 42 via an amendment dated January 4, 2010 was simply a narrowing of subject matter that had been present in the claims since the filing of this application.

Procedural history

On January 28, 2004, the above-referenced application was filed with 32 claims. The claimed application is generally directed to organ and tissue augmentation that utilizes two populations of cells with distinct functions, a first population of cells that is transiently transfected to express an angiogenesis modulating agent, and a second population of cells to be assimilated at the target site.

On January 27, 2005, a restriction requirement was issued. The restriction requirement required election of one of two inventions, claims drawn to a method of organ augmentation or claims drawn to a method of tissue repair. Via a telephone conversation with the Examiner, Applicants provisionally elected claims drawn to a method of organ augmentation with traverse. No further election was required. Original claims 1-13 and 23-29, drawn to a method of organ augmentation, were fully examined. Included in the original claims were claims 1 and 3-7, shown below.

1. A method of organ augmentation comprising the steps of:
transfecting a population of cells with a plasmid encoding an angiogenesis modulating agent; and
implanting the transfected cells into a target tissue region where the cells will express the angiogenesis modulating agent thereby inducing assimilation and differentiation of cells in the target region.

3. The method of claim 1, wherein the population of cells comprises undifferentiated cells.

4. The method of claim 1, wherein the population of cells comprises vascular endothelial cells (EC).

5. The method of claim 1, wherein the method further comprises co-administering a second population of cells.

6. The method of claim 5, wherein the second population of cells comprises undifferentiated cells.

7. The method of claim 5, wherein the second population of cells comprises vascular endothelial cells (EC).

On January 4, 2010, Applicants presented claim amendments to narrow the population of vascular endothelial cells in claim 7 to a population of *endothelial progenitor cells*, as well as new claims (dependent on claim 1 or independent claim 23) that recite the first or second population of cells comprises *endothelial progenitor cells* (claims 38, 39 and 42).

Subsequently, in the next Office Action dated March 30, 2010, the Examiner withdrew claims 7, 38, 39 and 42 as reciting endothelial progenitor cells. The Examiner stated that claims 7, 38, 39 and 42 were drawn to non-elected subject matter since "the populations of vascular endothelial cells and myoblasts have been constructively elected by original presentation for prosecution on the merits."

Pursuant to 37 C.F.R §1.111(b), on June 30, 2010, Applicants duly requested reconsideration of the restriction requirement. An Advisory Action dated July 15, 2010, maintained the restriction requirement.

Argument

There is no basis for the Examiner's assertion that "the species of vascular endothelial cells and myoblasts have been *constructively elected* by original presentation for prosecution on the merits." In fact, the original claims, including claim 5 (as shown above), recited "co-administering a second population of cells" – without restriction to vascular endothelial cells or myoblasts. Moreover, claim 6 (which was the subject of four prior Office Actions) further

defined the second population of cells to comprise "*undifferentiated cells*." Both of these claims encompass endothelial progenitor cells – and neither claim was the subject of a restriction requirement during the six-year pendency of this application. Hence, the Examiner's assertion of *constructive election* by the applicant is plainly incorrect.

Additionally, claim 7 originally recited that the second population comprises *vascular endothelial cells*. The amendment to which the Examiner objects would simply *narrow* this claim to *endothelial progenitor cells*. Applicant's specification clearly defines vascular endothelial cells as *including* endothelial progenitor cells. See, for example, paragraph [0120]:

> In another aspect of the present invention, tissue neovascularization can be enhanced using transient expression of VEGF and ***vascular endothelial cells (EC)*** within the tissue that incorporate into blood capillaries. ***Various types of EC including***, but not limited to, . . . ***progenitor EC . . . can be used*** for angiogenesis and vasculogenesis.

(Emphasis added.) See also, paragraph [0124]. Thus, the amendment to claim 7 does not switch species at all but rather simply narrows the claim. The same reasoning also applies to new claims 38-39 and 42.

In the Advisory Action dated July 15, 2010, the Examiner acknowledges that the first population of cells was originally claimed as undifferentiated cells (claim 3), vascular endothelial cells (claim 4) or myoblasts (claim 12) and the second population was originally claimed as undifferentiated cells (claim 6), vascular endothelial cells (claim 7) or myoblasts (claim 27). Despite the broad recitations of claims 3 and 6 to *undifferentiated cells*, she asserts without any explanation that the claims were constructively limited to vascular endothelial cells and myoblasts. However, the broadest claims to the present invention (claims 1 and 23), as originally filed and as they currently stands, simply claim a first population of cells (transiently infected to release an angiogenesis modulating agent) and a second population of cells (to be assimilated at the target site). At the time the initial restriction requirement was imposed, the Examiner did not require any restriction to a specific type of cells for either the first or the second population, much less to particular species of undifferentiated cells – or to vascular endothelial cells or myoblasts.

The Examiner further argued that endothelial progenitor cells cannot be accurately called a type of vascular endothelial cells. However, the claims need to be construed in light of the specification. As described in the specification in paragraph [0120], and reprised here, vascular endothelial cells (also called EC) are defined as:

> including, but are not limited to, human umbilical vein EC (HUVEC), human dermal microvascular EC (HDMEC), bovine aortic EC (BAEC), bovine capillary EC (BCE), ***progenitor EC***, and $CD34^+$ mononuclear cells.

Thus, the Examiner's conclusion that vascular endothelial cells are mature cells, distinct from undifferentiated progenitor endothelial cells is inconsistent with the teachings of the Applicant's specification.

Therefore, for at least the reasons set forth above, the restriction requirement should be withdrawn, and claims 7, 38-39 and 42 should be examined on their merits.

CONCLUSION

For all the reasons above reconsideration and withdrawal of the restriction requirement of March 30, 2010, as maintained in the Advisory Action dated July 15, 2010 are requested. The Director is hereby authorized to charge any deficiency in the fees filed with this paper, asserted to be filed with this paper or which should have been filed with this paper or any other paper in this application to our Deposit Account No. 141449, under Order No. 105447-2.

Dated: December 30, 2010

Respectfully submitted,

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